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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/920,272	08/22/97	MILLER	21451-B

HM11/1015

PATRICK J KELLY
SUITE 2600 ARAMARK TOWER
1100 MARKET STREET
PHILADELPHIA PA 19107

EXAMINER	
TENG, S	
ART UNIT	**PAPER NUMBER**
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/920,272	Applicant(s) Miller et al.
	Examiner Sally Teng	Group Art Unit 1646

☒ Responsive to communication(s) filed on *Aug 3, 1998* .

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-11 and 21-30* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11 and 21-30* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Claims 1-11 and 21-30 are pending in the instant application.

The rejection of claims 1-7, 11, 21, and 22 under § 112, second paragraph, is withdrawn.

2. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is vague and indefinite for recitation of "testing toxicity". It is not clear as to whether the cells are to be used to test the toxicity of a drug, the cells, or some other object. The claim does not recite the compound to be tested. Or does term "testing toxicity" refer to a specific assay?

3. Claim 28 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 28 is dependent from claim 24 which is directed to isolated precursor cells and does not encompass neurons, astrocytes, and oligodendrocytes.

4. The rejection of the claims under § 112, first paragraph, is partially withdrawn in view of the amendment. The portion of the rejection that is maintained is stated below.

Claim 11, 21-23, 29, and 30 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 11, 21-23, 29, and 30 are rejected because these claims include limitations encompassing therapeutic use of the isolated precursor cells. In fact, the claims specifically recite the use of the precursor cells or cells differentiated from the precursor cells for the treatment of specific diseases and disorders, for testing toxicity and for testing drug safety and efficacy. It is acknowledged that Example 16 shows successful transplantation of olfactory precursor cells into rat and successful differentiation of the cells into dopaminergic neurons. However, it is not predictable from Example 16 that transplantation of precursor cells of olfactory epithelium and tongue or cells differentiated from these precursor cells is effective in treating Parkinson's diseases. Example 16 only demonstrates that olfactory precursor cells can differentiate into dopaminergic neurons in rats. The treatment of neurodegenerative diseases and disorders and neurotrauma is complex. There is insufficient information from the prior art and from the specification for the use of the claimed precursor cells in the treatment of neurodegenerative diseases. It is not predictable that replacement of dead dopaminergic neurons with new ones is sufficient for treating neurodegenerative diseases. In fact, many neurodegenerative diseases are not associated with the death of dopaminergic neurons, for example, Alzheimers is associated with the degeneration of cholinergic neurons and ALS is associated with the progressive

degeneration of motor neurons. Moreover, many neurodegenerative diseases or injury to the CNS cannot be treated because of the intrinsic inability of neurons of the CNS to regenerate. Further, it is not predictable that the precursor cells of the tongue are characteristically the same as the precursor cells of the olfactory epithelium. Although it is acknowledged that the precursor cells of the tongue can differentiate into neurons, astrocytes, and oligodendrocytes, it is not clear as to what types of neurons, astrocytes, and oligodendrocytes, the precursor cells of the tongue differentiates into. The specification does not teach whether they are the dopaminergic neurons.

The claims also recite the use of the cells for testing toxicity, efficacy, and safety of drugs, but the specification does not provide assays for such tests. It is not predictable as how the precursor cells or the differentiated cells can be used to test drugs for the toxicity, safety, or efficacy of a drug, if it is not known whether the precursor cells can effectively treat a disease. Additionally, the specification does not correlate any *in vitro* drug assay using the claimed cells with *in vivo* use of the drug. Accordingly, the specification does not enable the use of the claimed cells in the recited methods.

Although the specification enables the claimed cells, the claims are rejected because they recite limitations for use of the cells which are not enabled by the specification.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-11, 21, 22, and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Calof et al.

Calof discloses isolation of precursor cells from mouse olfactory epithelium (page 117 and figure 1). Calof also discloses neurons differentiated from the olfactory epithelium and shows that these neurons express neuronal markers, NCAM a trophic factor(page 117). The precursor cells of Calof comprise both the neural stem cells and progenitor cells, since the stem cells produce new progenitor cells and the progenitor cells proliferate and differentiate into neurons. Although Calof does not disclose whether the neurons are dopaminergic and express glutamic acid decarboxylase, these are inherent properties of the neurons. Claims 21, 22, and 23 are included under this rejection because the claims are directed to precursor cells. The recitation of intended use as a limitation does not distinguish the claimed product from that disclosed in the prior art. Thus, the claims are anticipated by the prior art.

6. Claims 24-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Mayo et al.

Mayo discloses isolated precursor cells from mouse tongue (page 257 and figure 2) and cells differentiated from the precursor cells (figures 2-4). Although the reference does not disclose whether the precursor cells comprise the neural stem cells and neural progenitor cells, they must be present since the disclosed cells form the mouse tongue comprise neurons. Claims 29 and 30 are included under this rejection because the recitation of intended use as a limitation

does not distinguish the claimed precursor cells from those disclosed in the prior art. Thus, the claims are anticipated by Mayo et al.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Calof et al. in view of La Salle et al.

The teachings of Calof are discussed above. However, Calof does not disclose isolated precursor cells from olfactory epithelium transfected with a heterologous gene. La Salle teaches an adenovirus vector comprising the nucleic acid encoding β-gal for infection of primary culture

of sympathetic neurons (fig. 1). Accordingly, it would have been obvious to the skilled artisan at the time the invention was made to infect the precursor cells Calof with the adenovirus vector of La Salle, in order to obtain precursor cells expressing β-gal. The motivation to obtain precursor cells comprising the heterologous β-gal gene is for ease of tracking the precursor cells and the differentiated cells.

Thus, the claims are *prima facie* obvious over the prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sally Teng, Ph.D., whose telephone number is (703) 308-4230. The examiner can normally be reached on Mon.-Fri. from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2957.

Official papers filed by fax should be directed to (703) 305-3014. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

October 9, 1998

Sally Teng

SALLY TENG
PRIMARY EXAMINER